AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

Comparison of Automated Antimicrobial Susceptibility Testing Systems To Detect *mecC*-Positive Methicillin-Resistant *Staphylococcus aureus*

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KEYWORDS AST, *Staphylococcus aureus*, automated antimicrobial susceptibility testing, *mecC*, methicillin resistance

Methicillin resistance in *Staphylococcus aureus* is classically mediated by the *mecA* gene carried on a mobile genetic element, called staphylococcal cassette chromosome *mec* (SCC*mec*). *mecA* encodes an additional penicillin binding protein, named PBP2a, with low affinity for all beta-lactams except ceftaroline and ceftobiprole. A *mecA* variant, named *mecC*, which shares only 70% DNA sequence homology with *mecA*, was described in 2011 (1). Detection and identification of *mecC*-positive methicillin-resistant *Staphylococcus aureus* (MRSA) in the clinical microbiology setting are challenging and still require confirmation by a specific PCR (2). Cefoxitin has been reported to be more reliable than oxacillin for the detection of these strains by disc diffusion, broth microdilution, and agar dilution assays, with markedly differing performances observed between different brands of agar (3). Although automated systems are frequently used in routine laboratories for antimicrobial susceptibility testing (AST) due to their ease of use and cost-effectiveness, data concerning their ability to accurately classify *mecC*-positive MRSA are lacking. Using the Vitek 2 system (bioMérieux) and a collection of 62 *mecC*-positive MRSA isolates, Cartwright et al. showed that an atypical susceptibility profile (i.e., oxacillin susceptible/cefoxitin resistant) was associated with a sensitivity of 88.7% and a specificity of 99.5% for the identification of *mecC*-positive MRSA (4). The aim of the present work was to expand on these observations by comparing the performances of three commercially available automated AST systems using a large collection of clinical *mecC*-positive MRSA isolates from human and animal sources throughout Europe.

A total of 111 MRSA isolates of human and animal origin collected in different European countries (England, Scotland, Denmark, and France) confirmed as *mecC* positive by PCR (2) were included in this study. We compared the AST results obtained for oxacillin and cefoxitin with (i) the BD Phoenix PMIC/ID-60 panel (BD Diagnostic Systems, Franklin Lakes, NJ), (ii) the Vitek 2 AST-P581 card (bioMérieux, Marcy l'Etoile, France), and (iii) the

Accepted manuscript posted online 13 September 2017

Citation Kolenda C, Dupieux C, Decousser J-W, Larsen AR, Pichon B, Holmes M, Bès M, Teale C, Dickson E, Hill R, Skov R, Kearns A, Laurent F. 2017. Comparison of automated antimicrobial susceptibility testing systems to detect *mecC*-positive methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol 55:3554–3556. https://doi.org/10.1128/JCM.01150-17.

Editor Sandra S. Richter, Cleveland Clinic

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TABLE 1 Results of antimicrobial susceptibility testing of *mec C*-positive methicillin-resistant *Staphylococcus aureus* using three automated systems[a]

Automated system	No. (%) of strains with result:						
	Oxacillin		Cefoxitin		Beta-lactam susceptibility profile		
	S	R	S	R	Oxacillin-S/cefoxitin-S	Oxacillin-S/cefoxitin-R	Oxacillin-R/cefoxitin-R
MicroScan (Beckman Coulter)	111 (100.0)	0 (0)	4 (3.6)	107 (96.4)			
Vitek 2 (bioMérieux)	90 (81.1)	21 (18.9)	3 (2.7)	108 (97.3)	3 (2.7)	87 (78.4)	21 (18.9)
Phoenix (Becton, Dickinson)	94 (84.7)	17 (15.3)	28 (25.2)	83 (74.8)	28 (25.2)	66 (59.5)	17 (15.3)

[a]Abbreviations: S, susceptible; R, resistant. Breakpoints used were >2 mg/liter for oxacillin and >4 mg/liter for cefoxitin. The total number of *mecC*-positive methicillin-resistant *S. aureus* isolates was 111.

MicroScan Pos MIC type 31 panel (Beckman Coulter, Brea, CA). In accordance with CA-SFM/EUCAST and CLSI guidelines, the following breakpoints were used to assign methicillin resistance: >2 mg/liter for oxacillin and >4 mg/liter for cefoxitin.

Almost all *mecC* isolates were correctly identified as MRSA on the basis of cefoxitin when tested with Vitek 2 and MicroScan systems (97.3% and 96.4%, respectively), whereas 25.2% were found cefoxitin susceptible by Phoenix (Table 1). In agreement with previously reported data using the disc diffusion method (3), the majority of strains were oxacillin susceptible (81.1%, 84.7%, and 100% for Vitek 2, Phoenix, and MicroScan, respectively). All isolates assigned as cefoxitin susceptible were concomitantly detected oxacillin susceptible by the three automated systems. Extrapolating on the use of the oxacillin-susceptible/cefoxitin-resistant profile suggested by Cartwright et al. (4) as evocative of *mecC*-positive MRSA to the current data set, the percentage of strains matching that criterion of suspicion varied between the automated systems (96.4%, 78.4%, and 59.5% of the strains using MicroScan, Vitek 2, and Phoenix, respectively). Conversely, 15.3% and 18.9% of *mecC*-positive MRSA isolates were assigned as cefoxitin and oxacillin resistant by Phoenix and Vitek 2, respectively, while none showed resistance to both antibiotics with MicroScan, which is likely due both to the various levels of affinity of PBP2C for the different beta-lactams (5) and to the different levels of regulation of *mecC* by *mecI* and *mecR* (6).

This study, designed to compare three automated AST systems against a large number of *mecC*-MRSA isolates, shows that MicroScan and Vitek 2 give equivalent performance rates of >95% for the phenotypic detection of *mecC*-MRSA, which is comparable to those reported for the detection of *mecA*-MRSA (7–9). In contrast, while the Phoenix system gives a performance similar to those of other platforms for the detection of *mecA*-MRSA (8), the phenotypic detection rate for *mecC*-MRSA using the Phoenix system was low at 75%.

In conclusion, these results serve to highlight the fact that marked differences can be observed between different automated AST systems. Personnel working across the One Health agenda need to be aware of variable performances such as those described here so that informed decisions can be made, particularly for clinical diagnostic purposes. To date, published studies indicate that the prevalence of *mecC*-positive MRSA in humans and various animal species appears to be low (10). Nevertheless, the identification of multiple *mecC*-positive MRSA clones in various host species combined with their zoonotic risk suggests that the potential for expansion in human and/or animal reservoirs should not be ignored. Accordingly, we advocate the use of appropriate tools by those working across the One Health agenda to enable the effective detection of, and surveillance for, *mecC*-positive MRSA.

ACKNOWLEDGMENTS

We thank all the laboratory technicians who participated in the study and the French National Reference Centre for staphylococci.

This work was supported by Santé Publique France, the French agency for public health.

None of the authors have competing interests to declare.

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